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Thoracic fluid content by electrical cardiometry versus lung ultrasound score as predictors of weaning outcome in mechanically ventilated intensive care patients: A prospective cohort observational study

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Abstract
Background: Weaning individuals off mechanical ventilation (MV) is a pivotal choice in the intensive care unit (ICU). This work aimed to assess the precision of total thoracic fluid contents (TFC) using electrical cardiometry (EC) against the precision of lung ultrasound score (LUS) in forecasting weaning results in individuals on MV.
Methods: This prospective cohort observational work was performed on 85 subjects on MV for ≥ 48 hours aged ≥ 18 years old, both sexes, who met the weaning readiness requirements and had been planned for a spontaneous breathing trial (SBT).
Results: TFC before initiation of SBT and before extubation can significantly anticipate weaning outcomes in critical care unit patients on MV followed by LUS before the beginning of SBT and before extubation followed by rapid shallow breathing index (RSBI) before initiation of SBT and before extubation then cumulative fluid balance, while lung compliance before initiation of SBT and before extubation cannot predict weaning outcome. TFC, LUS, and RSBI before initiation of SBT and before extubation had been substantially decreased in successful weaning group compared to failed weaning group in studied patients ($P<0.05$). Cumulative fluid balance was significantly greater in the failed weaning group contrasted to successful weaning group ($P<0.05$).
Conclusions: TFC measured by EC has high predictive ability of weaning outcome in patients receiving MV than LUS, RSBI and cumulative fluid balance.

Keywords: Electrical cardiometry, thoracic fluid content, lung ultrasound score, weaning, mechanical ventilation

Introduction
Weaning individuals off mechanical ventilation (MV) is a crucial choice in the intensive care unit (ICU) [1]. It is advisable to wean patients off MV early to prevent difficulties triggered by prolonged MV; nevertheless, premature weaning may lead to extubation failure, that's independently linked to worse outcomes [2].
The first stage in the process of weaning involves checking for eligibility, accompanied by the spontaneous breathing trial (SBT) [3]. Multiple indicators must be meticulously evaluated before initiating SBT to guarantee sufficient ventilation, oxygenation, and airway reflexes [3]. Nevertheless, about one-third of recipients experience failure and need reintubation despite meeting all existing weaning prerequisites [4].
The lack of an optimal weaning metric to date may be attributed to the heterogeneity of critically sick subjects, which diminishes the prognostic accuracy of existing indicators across various subgroups of patients [5].
Currently, there is a growing interest in cardiac variables, including congestion in the lungs and hypervolemia, as contributory aspects to weaning failure [5]. Multiple methods have been previously documented for assessing volume status before the SBT, to identify individuals who might benefit from diuretic treatment [6]. Many of the previously utilised techniques needed either regular blood sampling, including brain natriuretic peptide [7], or skilled operators, like in echocardiography [8].
The Rapid Shallow Breathing Index (RSBI) is regarded as one of the most precise indicators

of weaning success. A cut-off value over 105 breaths/min/L was successfully utilised for foreseeing weaning trial failure [9].

Ultrasound is an effective technique for evaluating extra-vascular lung water (EVLW) [9]. Lung ultrasonography is regarded as an effective diagnostic and prognostic instrument for assessing different pulmonary diseases, particularly lung congestion [10]. Although ultrasound is precise and non-invasive, it remains a subjective, operator-dependent technique.

Thoracic fluid content (TFC) produced by electrical cardiometry (EC) is quantified using impedance cardiography technology, which evaluates TFC by analysing variations in the impedance of thoracic tissue to electric current. TFC encompasses the whole fluid component in the thorax, including intravascular, extravascular, and intrapleural fluids; hence, TFC is hypothesized to estimate extravascular lung water [11].

This work aimed to evaluate the precision of total TFC assessed by EC against the precision of lung ultrasound score (LUS) in forecasting weaning results in patients receiving MV.

Methods

This prospective cohort observational work had been done on 85 intensive care patients receiving MV for ≥ 48 hours aged ≥ 18 years old, both sexes, who met the weaning readiness requirements and had been planned for SBT employing pressure-supported ventilation. The study was done after approval from the Ethical Committee Tanta University Hospitals, Egypt (approval code: 35237/1/22) and registration of clinicaltrials.gov (ID: NCT05272982).

The criteria for exclusion included those having acute respiratory distress syndrome (ARDS), interstitial fibrosis of the lungs, pulmonary embolism, lung resection, fluid overload owing to cardiac, renal, or liver failure, cardiovascular patients with an ejection fraction (EF) below 40%, valvular or congenital cardiac conditions, cardiomyopathy, pericardial or pleural effusions, pneumothorax, pregnancies, and individuals with burns, injuries, or wounds that hindered the proper placement of the device electrodes or the US transducer, poor US image, and recent use of neuromuscular blocking agents (NMBAs) or steroids.

Each subject had been exposed to complete taking of history, clinical examinations, formal echocardiograms and chest imaging (chest X-rays, computed tomography scans) upon admission to the ICU, chest X-rays on the day of weaning, standard laboratory tests, as well as evaluation through lung ultrasound and electrical cardiometry.

Weaning readiness assessment

Sedatives were discontinued between 0.5 and 8 h before SBT (based on the sedative and duration of sedation). The determination of (readiness-to-wean) had been conducted by at least 2 ICU specialists depending on the protocol of the ICU. Weaning Criteria: Addressing the fundamental reason for intubation, Glasgow coma scale ≥12 and arousable, no additional requirement for ongoing sedative medications, adequate cough without excessive tracheobronchial secretions, no need for frequent suction, respiratory rate < 30 per minute, RSBI less than 105, fraction of inspired oxygen (FiO_2)≤ 0.4., arterial oxygen tension (PaO_2) > 60 mmHg, PaO_2/FiO_2 > 200 with positive end-expiratory pressure ≤ 8 cmH_2O, $PaCO_2$ normal or at baseline levels, adequate pH for patients' baseline respiratory condition, no indication of cardiac ischaemia, Stable cardiovascular status (heart rate (HR) ≤140 beats/minute and blood pressure sufficient with minimal or no vasopressors, with systolic Bl. Pr 90-160 mm Hg), no substantial electrolyte abnormalities and no fever. Patients meeting the requirements started a SBT after Ramsay sedation scale of (2 or 3). Where patients are cooperative, oriented and tranquil or responding to verbal commands only.

When one or more of the following criteria were met, weaning failure was defined as the need for reintubation within 48 h after extubation: tachypnea (respiratory rate greater than 35 breaths per minute), oxygen saturation below 90%, or PaO_2 below 60 mmHg on a fraction of inspired oxygen of forty percent, a discernible increase in the use of accessory respiratory muscles, visible facial signs of respiratory distress, and hemodynamic instability.

Spontaneous breathing trial (SBT)

The ventilator was configured to be pressure-supported mode for the SBT, with a pressure support of 5-8 cmH_2O and a positive end-expiratory pressure of 5 cmH_2O [12]. The SBT persisted for a duration of up to 30 minutes, after which the weaning parameters had been reassessed. Tidal volume should be at least 4 ml/kg and maximum inspiratory pressure (PI max) was (-20 to -25) cm H_2O. The extubation decision was made by 2 ICU specialists who were blinded to the TFC measurements.

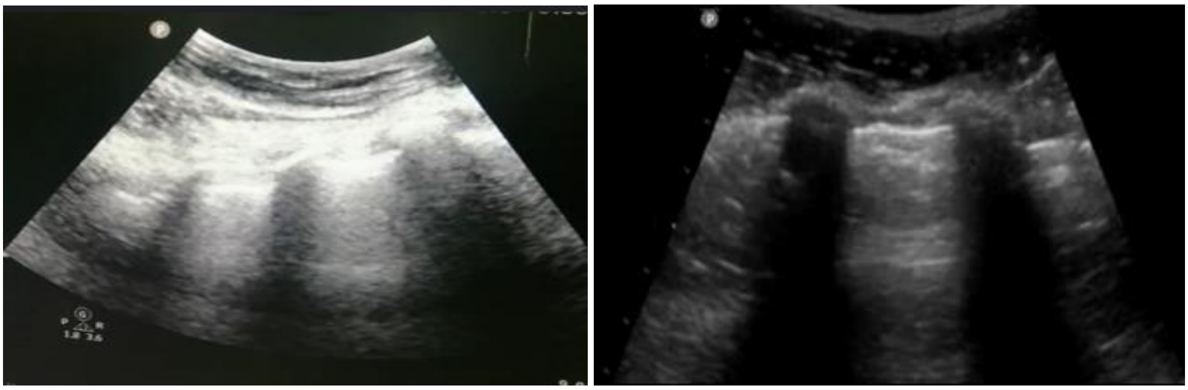
Thoracic fluid content by electrical cardiometry

TFC was measured using EC device (ICON ® Cardiotronics, Inc., La Jolla, CA 92307; Osyka Medical GmbH, Berlin, and Germany, model C3, Serial no: 1725303). The ICON instrument was linked to 4 electrocardiogram electrodes, positioned on the patients' skin following alcohol cleansing, at the neck beneath the left ear, approximately above the left clavicular midpoint, and two electrodes along the left mid-axillary line, one at the xiphoid process level and the other 5 cm inferior to this point. The TFC was observed for 30s, and the average value was recorded before initiation of SBT and before extubation.

Ultrasound examination

The 12-region method for pulmonary evaluation was conducted with the Philips® (CX50 - Extreme edition) with a phased array transducer. The haemithorax was partitioned into 6 zones: 2 anterior zones (located between the midaxillary and parasternal lines), 2 lateral zones (situated between the midaxillary and posterior axillary lines), and 2 posterior zones (positioned beyond the posterior axillary lines). Patients were investigated in a supine posture for lateral and anterior zones then tilted into lateral position for examination of posterior zones after securing the endotracheal tube.

The B-line is characterized as a laser-like vertical hyperechoic artefact that stretches from the pleural line to the screen' bottom and shifts with respiratory motions. Two categories of B-lines were assessed: B-7 lines indicate interstitial edema, spaced 7 mm apart, whereas B-3 lines denote alveolar edema, spaced 3 mm apart. The LUS was computed for each subject as follows: The 12 intercostal areas were examined vertically from top to bottom, and an A B-line score was assigned to each zone as the following: 0: no lines, 1: 7 B-lines, 2: 3 B-lines, and 3: consolidation. The total LUS was determined by summing all zones of the lungs, ranging from 0 to 36. The LUS was observed before initiation of SBT and before extubation. Figure 1.



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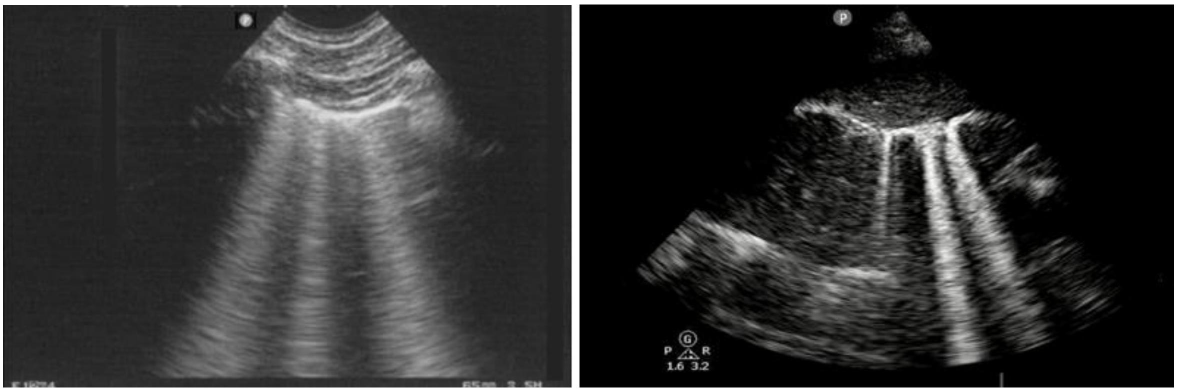

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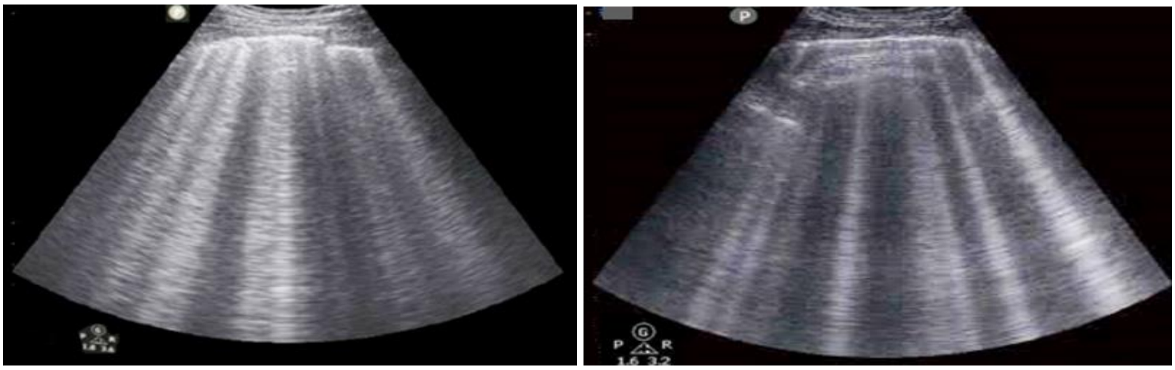


C

Fig 1: Lung ultrasound (A) normal lung, (B) B7 lines denoting interstitial lung edema and (C) B3 lines (alveolar edema)

RSBI was calculated by dividing respiratory rate/tidal volume. Lung compliance was also recorded before initiation of SBT and before extubation. Cumulative fluid balance (equals the total fluid intake minus the total fluid output for the duration from ICU admission to the time of initiation of SBT) and fluid balance at the day of SBT were recorded.

The primary outcome was to compare the area under the curve (AUC) of the receiver operating characteristic (ROC) for TFC and LUS in anticipating weaning outcomes among subjects receiving MV. The secondary result was a comparison with other weaning measures, including RSBI, lung compliance, and cumulative fluid balance.

Sample Size Calculation: The sample size calculation was done by MedCalc Software Ltd v. 20 with 80% power, 5% confidence limit, the expected AUC of the ROC curve of the predictive ability for the TFC in predicting weaning failure was at least 0.69 and the null hypothesis AUC of the ROC curve was 0.5 according to a previous study [13]. Four cases were added to overcome dropout. Therefore, 50 patients were recruited in the study.

Statistical analysis: Statistical analysis had been conducted employing SPSS v26 (IBM Inc., Chicago, IL, USA). Quantitative parameters had been displayed as mean and standard deviation (SD) and contrasted among both groups utilizing an unpaired Student's t-test. Qualitative parameters had been displayed as frequency and percentage (%) and analyzed employing the Chi-square or Fisher's exact test when appropriate. ROC curve had been utilized for evaluation of diagnostic performance sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV). A two-tailed P value < 0.05 was considered statistically significant.

Results

One hundred six individuals had been evaluated for eligibility; 13 patients didn't satisfy the requirements, and 8 patients had their next of kin decline participation in the research. All assigned patients were monitored and subjected to statistical analysis. Figure 2.

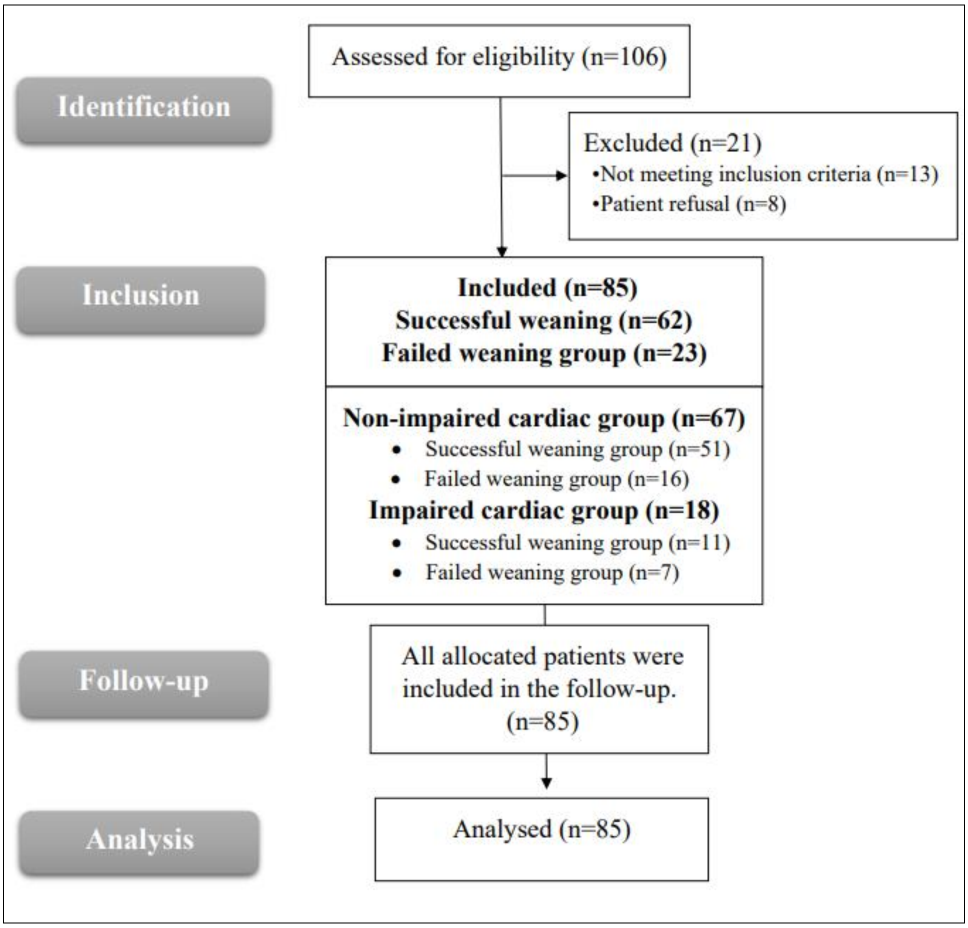


Fig 2: STROBE flowchart of the enrolled patients

Patient characteristics including (age, sex and APACHE II), comorbidities including (DM, HTN, smoker and asthma) duration of MV and fluid balance at the day of SBT were insignificantly varied among the two groups. COPD and cumulative fluid balance were significantly greater in the failed weaning group contrasted to successful weaning group (*P*<0.05). Table 1.

Table 1: Patient characteristics, comorbidities, duration of MV, fluid balance at the day of SBT and cumulative fluid balance of the studied patients

		Successful weaning patients (n=62)	Failed weaning patients(n=23)	P
Age (years)		47.82±16.53	50.65±16.74	0.487
Sex	Male	33(53.23%)	14(60.87%)	0.529
	Female	29(46.77%)	9(19.57%)	
APACHE II		8.77±4.14	7.35±3.13	0.138
Comorbidities	DM	20(32.26%)	8(34.78%)	0.826
	HTN	23(37.1%)	9(39.13%)	0.863
	Smoker	25(40.32%)	10(43.48%)	0.793
	COPD	8(12.9%)	9(39.13%)	0.007*
	Asthma	2(3.23%)	2(8.7%)	0.290
Duration of MV (days)		3.24±0.78	3.78±1.81	0.057
Fluid balance at the day of SBT (ml)		509.68±345.32	673.91±353.19	0.056
Cumulative fluid balance (ml)		411.29±348.35	595.65±333.68	0.031*

Data are presented as mean ± SD or frequency (%). *Significant as P value≤0.05, APACHE: Acute physiology and chronic health evaluation, DM: Diabetes mellitus, HTN: Hypertension, COPD: Chronic obstructive pulmonary disease, MV: mechanical ventilation, SBT: spontaneous breathing trial.

Lung compliance, P/ F ratio before initiation of SBT and before extubation were insignificantly different between both groups. TFC and LUS before initiation of SBT and before extubation were significantly decreased in Successful weaning group contrasted to failed weaning group in studied patients (*P*<0.05). Table 2

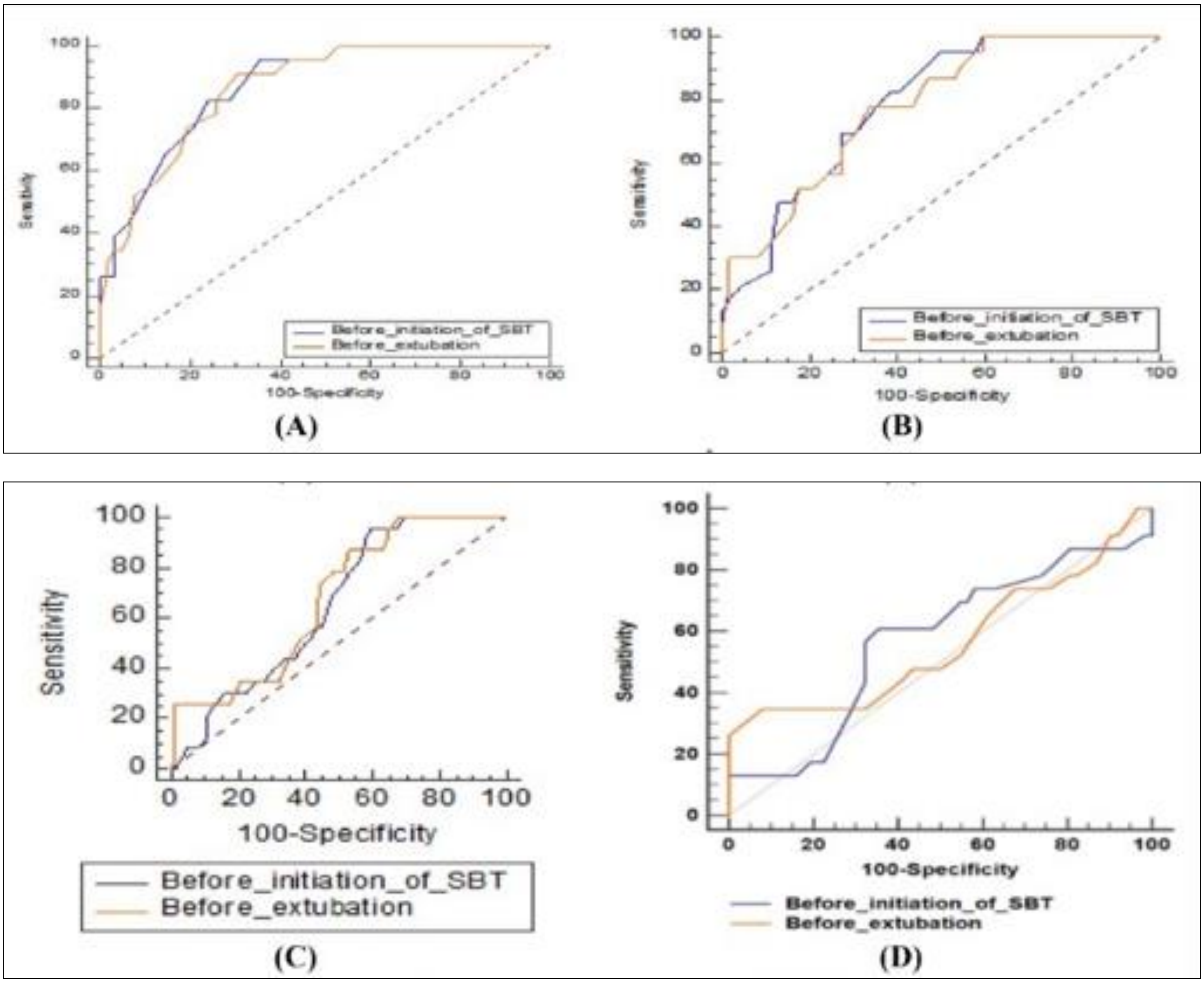
Table 2: Lung compliance, P/F ratio, TFC and LUS of the studied patients

		Successful weaning patients (n=62)	Failed weaning patients (n=23)	P
Lung compliance (ml/cm H_2O)	Before initiation of SBT	52.65±7.12	51.3±9.45	0.483
	Before extubation	54.26±6.75	50.13±12.39	0.053
P/F ratio	Before initiation of SBT	334.6±50.86	326.65±62.75	0.550
	Before extubation	262.05±23.84	270.04±42.39	0.277
TFC (KOhm-1)	Before initiation of SBT	34.98±7.33	46.39±6.54	<0.001*
	Before extubation	34.98±7.53	46.22±6.2	<0.001*
LUS	Before initiation of SBT	14.63±7.6	19.83±5.33	0.003*
	Before extubation	14.52±7.45	20.39±5.37	0.001*

Data are presented as mean ± SD or frequency (%). *Significant as P value≤0.05, LUS: Lung ultrasound, TFC: thoracic fluid content.

TFC, LUS and RSBI before initiation of SBT can significantly predict weaning outcome respectively (*P*< 0.001,0.002 and 0.015 and AUC = 0.871,0.680 and 0.647) at cut-off >40, >16 and >72 with 82.61%,78.26% and 43.48% sensitivity, 75.81%, 56.45% and 66.13% specificity, 55.9%, 40% and 32.3% PPV and 92.2%, 87.5% and 75.9% NPV in studied patients.

TFC, LUS and RSBI before extubation can significantly predict weaning outcome respectively (*P*< 0.001, <0.001 and 0.005 and AUC = 0.866, 0.714 and 0.673) at cut-off >39, >14 and >70 with 91.30%, 86.96% and 52.17%sensitivity, 69.35%, 53.23% and 61.29% specificity, 52.5%, 40.8% and 33.3% PPV and 95.6%, 91.7% and 77.6% NPV in studied patients. Cumulative fluid balance can significantly predict weaning outcome (P = 0.038 and AUC = 0.639) at cut-off >500 with 60.87% sensitivity, 62.90% specificity, 37.8% PPV and 81.3% NPV. While lung compliance before initiation of SBT and extubation can't predict weaning outcome respectively (P = 0.352, 0.437 and AUC = 0.568, 0.562) at cut-off ≤53, ≤55 with 69.57%, 52.17% sensitivity, 45.16%, 45.16% specificity, 32%, 26.1% PPV and 80%, 71.8%NPV. Figure 3.



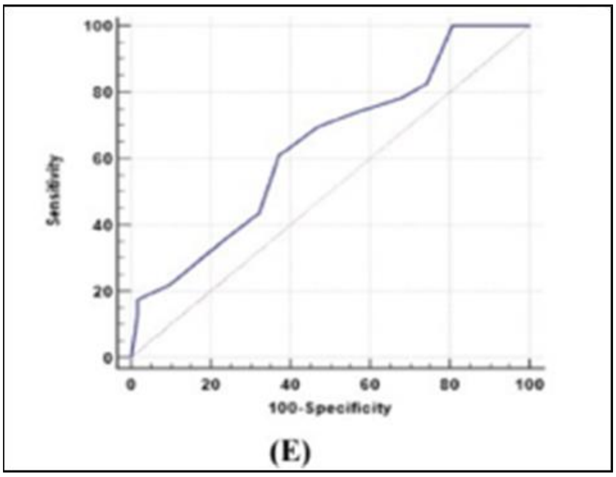


Fig 3: ROC curve of (A) Thoracic fluid content, (B) lung ultrasound score and (C) rapid shallow breathing index, (D) lung compliance before initiation of SBT and before extubation, and (E) cumulative fluid balance in prediction of weaning outcome in studied patients

Based on AUC, TFC before initiation of SBT and before extubation can significantly predict weaning outcome (*P*<0.001and AUC= 0.871 and 0.866) followed by LUS before initiation of SBT and before extubation (P=0.002 and <0.001 and AUC= 0.680 and 0.714) followed by RSBI before initiation of SBT and before extubation (P=0.015 and 0.005 and AUC= 0.647 and 0.673) then cumulative fluid balance (P=0.038 and AUC= 0.639), while lung compliance before initiation and extubation of SBT can't predict weaning outcome. Figure 4.

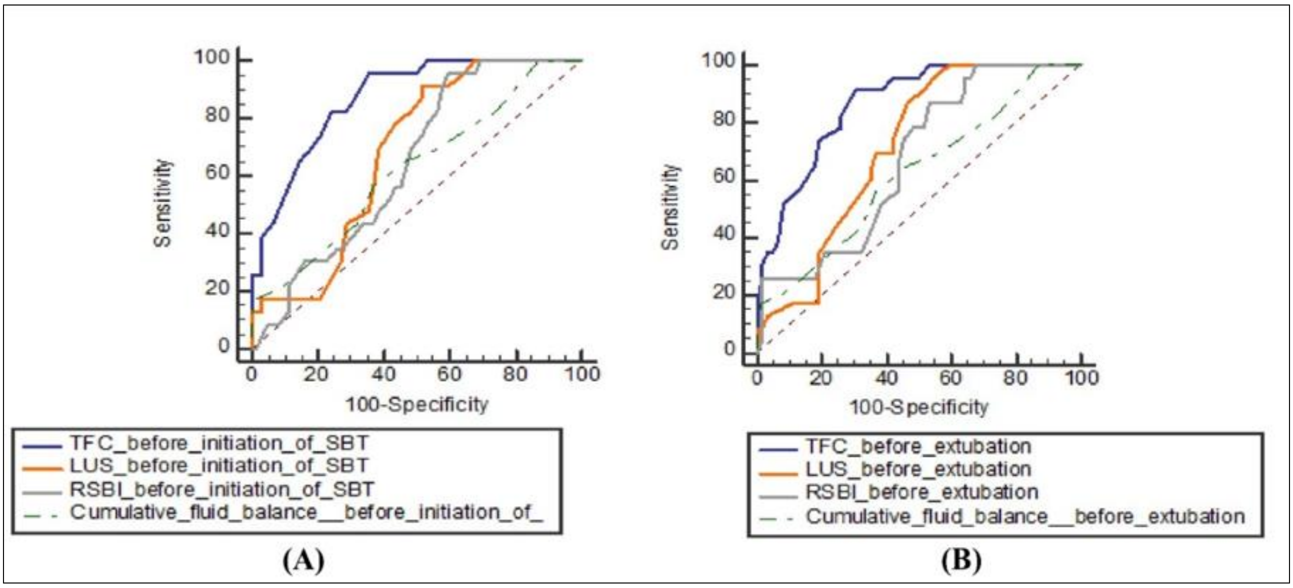


Fig 4: ROC curve of comparison between the role of thoracic fluid content, lung ultrasound, rapid shallow breathing index (A) before initiation of SBT and (B) before extubation, and cumulative fluid balance in prediction of weaning in mechanically ventilated patients

Discussion

The adverse effects of extended mechanical breathing on survival and disability have been noted [14]. It is essential to extubate the patients promptly once they are prepared. Nonetheless, premature removal from the ventilator heightens the likelihood of extubation failure, that happens in 10-25% of subjects [15] and is linked to considerable morbidity and death [16].

In our study, the duration of MV and fluid balance at the day of SBT were insignificantly varied among the two groups. This was in agreement with Joussellin *et al.* [17] who estimated lung aeration by chest electrical impedance tomography and lung US throughout extubation in 40 patients in a medical ICU and reported that days of ventilation before extubation and 24 h fluid balance, were insignificantly different between successful and failed weaning groups.

In our results, cumulative fluid balance was significantly greater in the failed weaning group contrasted to successful weaning group. Supporting our results, Ghosh *et al.* [18] who examined the influence of accumulated fluid balance on extubation failure after scheduled extubation. 201 MV ICU patients for at least 24 h were prospectively evaluated. Also, Upadya *et al.* [7] who measured the correlation between fluid balance and weaning outcome in 87 MV patient and found that cumulative fluid balance was substantially higher in weaning failures than successes.

According to our results, cumulative fluid balance can significantly predict weaning outcome (P = 0.038 and AUC = 0.639) at cut-off >500 with 60.87% sensitivity, 62.90% specificity, 37.8% PPV and 81.3% NPV. Our results agreed with Wang *et al.* [19] who conducted anested case control study investigating The dose-response connection between fluid balance and ventilator-associated events indicated that a positive fluid balance, rather than a negative one, heightened the risk of such events, with an increasing positive fluid balance correlating with a greater likelihood of ventilator-associated occurrences. Consistent with our findings, Ghosh *et al.* [18] showed that the AUC for cumulative balance in predicting extubation failure was 0.6 (95% CI: 0.504-0.697), with an appropriate cutoff value of 3490 ml, yielding sensitivities and specificities of 60% and 59.5%, correspondingly.

According to our results, RSBI before initiation of SBT and before extubation were significantly lower in successful weaning group than failed weaning group. In contrast, Fathy *et al.* [5] who evaluated the accuracy of TFC as a predictor of weaning outcome in 64 critically ill surgical patients who were eligible for extubation and reported that RSBI before initiation of SBT was insignificantly different between failed and successful weaning groups. In line with our results, Souza *et al.* [20] who conducted a work on tracheostomized individuals who were receiving MV for > 14 days and met the criteria for weaning and he found that The sequential assessment of the ventilatory pattern and the examination of RSBI fluctuations seem to forecast the unsuccessful weaning from MV in tracheostomized subjects.

In our study, lung compliance before initiation of SBT and before extubation were insignificantly varied among the two groups. Comparable to our results, Fathy *et al.* [5] who stated that compliance was insignificantly different between both failed and successful weaning groups. However, Abplanalp *et al.* [21] who conducted across sectional multi-institutional study of 2.337 MV subjects aged >18 years with documented SBT and extubation trial and showed that compliance of lungs was a significant predictor for failure of the extubation. The different sample size may explain the difference between their and our results.

Our results revealed that P/F ratio before initiation of SBT and before extubation were insignificantly different between both groups. Our results agreed with Fathy *et al.* [5] who revealed insignificant difference between both failed and successful weaning groups regarding P/ F ratio before initiation of SBT. In disagreement with our results, El-Beheidy *et al.* [22] who conducted a cross-sectional work on 53 children hospitalized at PICU aged < 18 years subjected to MV showed that P/F ratio before initiation of SBT was significantly greater in successful weaning group contrasted to failed weaning group. Younger age of their patients (inclusion of pediatric cases only in their study versus adult cases in ours) may explain this difference from our results.

Our results showed that TFC before initiation of SBT and before extubation were substantially decreased in successful weaning group contrasted to failed weaning group. Our results are comparable with Fathy *et al.* [5] who revealed that TFC was greater in the failed SBT group contrasted to the successful SBT group.

Our results about TFC before initiation of SBT and before extubation are supported by Fathy *et al.* [5] who reported moderate predictive ability for TFC in prediction of weaning failure (AUC [95% CI] 0.69 [0.57- 0.8], positive predictive value 60%, negative predictive value 79.5%, cutoff value > 50 $k\Omega^{-1}$).

In our study LUS before initiation of SBT and before extubation were substantially decreased in successful weaning group contrasted to failed weaning group. Our results are supported by Joussellin *et al.* [17] who documented that lung aeration (LUS score and posterior LUS score) were significantly lower in extubation success than extubation failure groups (LUS scorewas 10 (6-15) vs 19 (14-22); p= 0.003) and posterior LUS score was (5 (2-7) vs. 8 (7-10); P= < 0.001) in extubation success vs extubation failure groups). Also, Bouhemad *et al.* [23] who determined whether LUS alone might detect older patients at elevated risk of weaning or failure of extubation. LUS and TTE had been carried out in 40 subjects before and at the end of SBT and reported insignificant difference among groups in LUS scores before SBT while significant differences in all (global and anterolateral scores) LUS scores were observed between the failed groups and the success group after the SBT.

In agreement with our findings about LUS before initiation of SBT, Enghard *et al.* [24] who evaluated the role of lung US and transpulmonary thermodilution measure to detect the pulmonary fluid condition in 50 MV subjects in ICU and stated that LUS of 18.5 precisely predicted severely elevated EVLW in critically ill subjects receiving MV. Also, Zhao *et al.* [25] who studied the prognostic value of EVLW assessed with LUS in 21 subjects with ARDS and pulse index continuous cardiac output (PICCO) and stated that LUS of 16.5 is a very efficient prognostic marker among subjects with ARDS.

Limitations of the study included that the sample size was relatively small. The study was in a single center not comparing our findings with other local anesthetics and different doses and concentrations and lacked the prediction of mortality and hospital stay.

Conclusions

TFC measured by EC has a higher predictive ability of weaning outcome in subjects receiving MV than LUS and cumulative fluid balance. TFC can overcome the intrinsic limitations of ultrasound and can preferably and effectively replace it. Lung ultrasound is difficult in obese patients, with subcutaneous emphysema, and large thoracic dressing and it is operator dependent.

List of Abbreviation

- **MV:** Mechanical ventilation
- **ICU:** Intensive care unit
- **TFC:** Thoracic fluid contents
- **EC:** Electrical cardiometry
- **LUS:** Lung ultrasound score
- **SBT:** Spontaneous breathing trial
- **RSBI:** Rapid shallow breathing index

Declarations

Ethics approval and informed consent

The study was done from March 2022 to February 2023 following permission from the Ethical Committee. (approval code: 35237/1/22) and registration of clinicaltrials.gov (ID: NCT05272982). An informed written consent had been obtained from the next kin of patient.

Consent for publication

Not Applicable.

Data availability

Data is available upon reasonable requests from corresponding author.

Competing interests

The authors have no financial or proprietary interest in any material discussed in this article.

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No funding was received for conducting this study.

Authors' contributions

All authors contributed to the study conception and design. Material preparation, data collection and analysis were performed by [E.R.A.], [N.H.F.], and [G. F. E.]. The first draft of the manuscript was written by [G. M. E.] and [M. I. M. E.]. All authors commented on previous versions of the manuscript. All authors read and approved of the final manuscript.

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There is none to be declared

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